REMARKS

Claims 21-24 and 29-30 are currently pending in this application. Claims 25-28 have been canceled as directed to non-elected subject matter, without admission and without prejudice to Applicants' right to pursue the subject matter of those canceled claims in either this or other (e.g., related continuing or divisional) patent applications.

Claim 21 has been amended to recite a method "for enhancing a pre-existing immune response." Support for this amendment can be found in the specification at page 2, lines 9-12. Claim 21 has further been amended to recite "contacting an antibody" rather than "administering an antibody." Support for these amendments can be found in the specification at page 16, line 11 to page 17, line 11.

Claims 22-24 have been amended to correct obvious typographical errors.

No new matter has been introduced in these amendments. Upon entry of these amendments, claims 21-24 and 29-30 will be pending. Entry and consideration of these amendments is respectfully requested.

Objection to Formal Drawings

In the Office Action, the Examiner has maintained his objection to the drawings. Formal drawings correcting the deficiencies noted by the Examiner are submitted with this Response (Figures 1a-5b on ten (10) sheets).

Rejection under 35 U.S.C. § 112, first paragraph, enablement

The Examiner has rejected claims 21-24 and 29-30 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. The Examiner alleges that *in vitro* and animal model studies do not correlate well with *in vivo* clinical trial results in patients. The Examiner argues that, in the absence of *in vivo* clinical data, it would be too unpredictable to determine the efficacy of a therapeutic strategy, and that the specification does not enable a person of ordinary skill in the art to practice the invention.

Applicants note that claim 21 has been amended to recite "enhancing a pre-existing immune response" and "contacting an antibody" rather than "administering an antibody." The specification clearly describes induction of mature antigen presenting cells ("APCs") by contacting them with antibodies. See specification at page 16, line 11 to page 17, line 11. The specification also clearly recites the use of antibodies to enhance a pre-existing immune response. See specification at page 2, lines 9-12. Accordingly, Applicants respectfully submit that claims 21-24 and 29-30, as amended, are enabled in light of the specification, and request withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, first paragraph, written description

The Examiner has rejected claims 21-24 and 29-30 under 35 U.S.C. § 112, first paragraph, for alleged lack of written description. The Examiner alleges that the limitation "without blocking of CD40L" lacks support in the specification as filed.

Applicants respectfully point out that claim 21 has been amended to recite "without completely blocking binding of CD40L to CD40." See Examples 4 and 5 at pages 22-23. The specification clearly describes partial blocking of CD40L by up to 88%. *Id.* Accordingly, Applicants submit that the rejection for lack of written description has been obviated, and respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, second paragraph, indefiniteness

The Examiner has rejected claim 24 for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner argues that the trade name "DeImmunized™" is indefinite, because the trade name identifies the source of the product and not the product itself.

Applicants respectfully disagree with the Examiner, and would like to point out that DeImmunized™ is not a product, but a method of treating antibodies. The term DeImmunized™ is clearly defined at page 8, lines 10-14. The method of treating the antibodies is outlined in the cited application, which is incorporated by reference and need not be repeated in the present

specification. Applicants therefore respectfully submit that the rejection under the second paragraph of 35 U.S.C. § 112 has been obviated, and should be withdrawn.

Rejection under 35 U.S.C. § 102(e)

The Examiner has rejected claims 21-24 and 30 under 35 U.S.C. § 102(e) as allegedly anticipated by Melief *et al.* (US 2003/0022860) ("Melief"). The Examiner argues that Melief teaches the use of agonistic anti-CD40 antibodies for enhancing immune responses.

Anticipation requires that each and every element of the rejected claim(s) be disclosed in a single prior art reference. See M.P.E.P. § 2131 (8th Ed. Rev. 2, May 2004). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Every element of the claimed invention must literally be present, arranged as in the claim. *Perkin Elmer Corp. v. Computervision Corp.*, 732 F.2d 888, 894, 221 USPQ 669, 673 (Fed. Cir. 1984).

As pointed out by the Examiner, Melief does not disclose "without blocking binding of CD40L to CD40." Accordingly, Applicants submit that Melief does not teach all of the limitations of claims 21-24 and 30, and thus cannot anticipate the present invention. Additionally, Melief administers a CD40 binding molecule together with a CTL activating peptide, and thereby induces an exogenous antigen-specific immune response. See Melief at paragraphs 47-48. In contrast, the present invention teaches the enhancement of an immune response to antigens already present on the antigen presenting cells ("APC"). See specification at page 17, lines 2-3. Rather than modifying the antigen repertoire of the APC by utilizing an exogenous antigen, the present invention *enhances pre-existing immunity*. Melief does not teach or suggest the use of agonistic anti-CD40 antibodies for enhancing *pre-existing* immune responses. In the interest of expediting prosecution, and in order to more clearly illustrate this difference, claim 21 has been amended to recite a method "for enhancing a pre-existing immune response." Support for this amendment can be found in the specification at page 2, lines 9-12. Accordingly, Melief does not teach every element of the claims, as amended, and cannot anticipate the present invention.

In view of the foregoing arguments, Applicants respectfully submit that claims 21-24 and 30 are not anticipated by Melief. Applicants respectfully request that the rejection under 35 U.S.C. § 102(e) be withdrawn.

Rejections under 35 U.S.C. § 103(a)

The Examiner has rejected claims 21-24 and 30 under 35 U.S.C. § 103(a) as allegedly obvious over Melief in view of Zhou *et al.* (Hybridoma 1999, 18:471-488) ("Zhou") and/or Caux *et al.* (*Research in Immunology* 1994, 145:235-239) ("Caux") and/or Katira *et al.* (Leukocyte Typicng V, Schlossman *et al.*, Ed.) ("Katira") and/or Schwabe *et al.* (*Hybridoma* 1997, 16:217-226) ("Schwabe"). The Examiner alleges that Melief teaches methods of treating tumors or infectious diseases comprising adminstering anti-CD40 antibodies or fragments to generate or enhance immune responses. In particular, the Examiner argues that Melief discloses the anti-CD40 antibody FGK-45, and that the remaining references teach that a number of agonistic anti-CD40 antibodies were well-known in the art. The Examiner alleges that it would be obvious to combine the teachings of Melief and, for example, Schwabe, to reach the present invention.

The Examiner has also rejected claim 29 under 35 U.S.C. § 103(a) as allegedly obvious over Melief in view of Zhou and/or Caux and/or Katira and/or Schwabe as applied above, and further in view of Maraskovsky *et al.* (U.S. Patent No. 6,497,876) ("Maraskovsky"). The Examiner alleges that Maraskovsky teaches the missing limitation of the use of interferon-γ to treat tumors and infections. The Examiner argues that it would be obvious to combine the teachings of these references to reach the present invention.

To establish a *prima facie* case of obviousness, the Examiner must meet three criteria. The Examiner must establish that (1) there is some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there is a reasonable expectation of success; and (3) the prior art reference (or references when combined) teach or suggest all the claim limitations. See MPEP 706.02(j) and 2143. The teaching or suggestion to make the claimed combination and the

reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q2d 1438 (Fed. Cir. 1991).

As argued above, Applicants respectfully submit that Melief administers a CD40 binding molecule together with a CTL activating peptide, and thereby induces an exogenous antigen-specific immune response, and does not teach or suggest the enhancement of a *pre-existing* immune response. Similarly, none of the additional references cited teach or suggest the enhancement of a pre-existing immune response. The remaining references (Zhou, Caux, Katira, Schwabe, and Maraskovsky) fail to provide the missing limitation, and provide no suggestion or motivation to combine with Melief, or any other reference, to enhance a pre-existing immune response. The Examiner has failed to satisfy the first and third prongs of the test outlined above, and accordingly, has not established a *prima facie* case of obviousness.

Additionally, Applicants submit that the present invention displays unexpected results, because the finding that the use of an antibody directed against human CD40 enhances *pre-existing* immunity is not disclosed or suggested in the prior art.

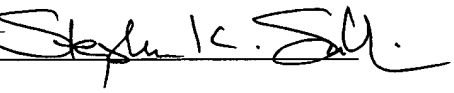
In view of the foregoing, Applicants respectfully submit that claims 21-24 and 29-30 are non-obvious. Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

In view of the above amendments and remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue. If there are any other issues remaining which the Examiner believes could be resolved through a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Dated: April 27, 2005

Respectfully submitted,

By 

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Attachments